

## REMARKS

Claims 1-49 were pending in this application. Claims 37 and 48 have been canceled. Claims 1, 23, 34 and 38 have been amended to clarify that the component is a supermolecular structure formed by a plurality of molecules and/or to correct typographical errors. These amendments are supported throughout the specification, and particularly at page 27, lines 34-36 of the application as filed, and add no new matter.

### Restriction Requirement

The Examiner has required restriction of the claims under 35 U.S.C. §§ 121 and 372. More specifically, the Examiner has required restriction to one of the following groups:

Group I	Claim(s) 1-33, 44, 45 and 49, drawn to an assembly comprising a gas-filled microvesicle.
Group II	Claim(s) 34-37, drawn to a kit.
Group III	Claim(s) 38-43 and 48, drawn to a method for preparing an assembly.
Group IV	Claim 46, drawn to a method of ultrasonic imaging.
Group V	Claim 47, drawn to a method of therapeutic treatment.

The Examiner asserts that the inventions of Groups I-V do not relate to a single general inventive concept under PCT Rule 13.1 because they allegedly lack the same or corresponding special technical features. Applicants respectfully traverse. The currently pending claims, relating to an assembly, a kit, a method for preparing and assembly, a method of ultrasonic imaging or a method of therapeutic treatment were properly deemed to comply with the PCT rules during the international phase and the instant restriction requirement appears to violate PCT Article 27(1): *no national law shall require compliance with requirements relating to the form or contents of the international application different from or additional to those which are provided for in this Treaty and the Regulations.*

Further Applicants submit that contrary to the Examiner's assertion, **all** of the pending claims **do** share the same special technical features: all require an assembly comprising a gas-filled microvesicle bearing a first overall net charge and a component associated with said microvesicle wherein said component is a supermolecular structure formed by the association of a plurality of molecules, bears a second overall net charge opposite in sign to said first net charge and comprises a targeting ligand, a diagnostic agent or any combination thereof, and a biocompatible surface active agent. The claimed compositions are not disclosed or suggested in the cited art. While the Examiner alleges Cravenness (US 2002/0102217, hereafter "Klaveness") teaches targeted multiple-specific gas-containing microbubbles of

DSPS (i.e. anionic) coated non-covalently with polylysine (i.e. cationic) and a fusion peptide comprising a PS binding component and a fibronectin peptide sequence, this construct does not include the special technical features of the claims. In particular, Klaveness does not disclose a component to be associated with the microvesicle comprising a biocompatible surface agent. Indeed, Klaveness teaches only polylysine and a fusion peptide. Moreover, as the instant amendment clarifies, the claims require that the component is a supermolecular structure formed by the association of a plurality of molecules (comprising surface active agent molecules). This feature is neither taught nor suggested by Klaveness. In particular, Klaveness Example 4 cited by the Examiner, the material forming the microbubbles (DSPS) and the materials alleged to provide the non-covalent coating (polylysine and fusion peptide) are admixed together in the preparation, and thus cannot form two separate structures (e.g. microvesicles and the associated supermolecular component) required by the instant claims. Thus the instant claims are novel and unobvious over the prior art, are in compliance with PCT Rule 13.1 and 13.2 and restriction is improper.

However, for the purposes of submitting a complete response, Applicants hereby elect Group I – Claims 1-33, 44, 45 and 49, drawn to an assembly comprising a gas-filled microvesicle, with traverse.

#### **Species Election Requirement**

The Examiner has required election of the following species:

i)	a <i>specific</i> chemical species corresponding to a constituent which imparts a first overall net charge to the microvesicle.
ii)	a <i>specific</i> chemical species corresponding to the component associated with the microvesicle that bears a second overall net charge that is opposite in sign to the first overall net charge.
iii)	a <i>specific</i> chemical species to represent a diagnostic or therapeutic agent.
iv)	a <i>specific</i> chemical species to represent a surface active agent.

Applicants respectfully traverse the species election. For the reasons explained in connection with the restriction requirement, the claimed species are believed to be in full compliance with the PCT rules and to share the same special technical features. Consequently Applicants submit that the species election is improper.

Additionally Applicants note that the claims require a targeting ligand, a diagnostic agent or a combination thereof and thus presumably item iii) of the species election requirement should require a specific targeting agent, diagnostic agent or combination thereof.

However, for the purposes of submitting a complete response, Applicants elect the following species with traverse:

- i) lipid bearing positive charge (claim 26), in particular “tertiary or quaternary ammonium salts comprising at least one (C<sub>10</sub>-C<sub>20</sub>) acyl chain linked to the nitrogen atom through a (C<sub>3</sub>-C<sub>6</sub>) alkylene bridge” (claim 27) more specifically (DSTAP (1,2-Distearoyl-3-trimethylammonium-propane chloride) page 31, line 18 and Example 2, 4 ;
- ii) polyethyleneglycol modified phospholipid (claim 24); in particular phosphatidylethanolamines modified with polyethyleneglycol (page 16, line 6)), more specifically DSPE-PEG (Example 7)
- iii) targeting ligand: peptide (claim 2)
- iv) phospholipids (claim 11).

Applicants identify claims 1-2, 4-18, 22-27, 30-33, 44-45, and 49 from Group I as reading on the elected species.

#### **Potential Rejoinder**

If the restriction requirement is maintained despite Applicants traversal, Applicants request rejoinder of the dependent method claims at the appropriate time.

No fee is believed to be necessary in connection with the filing of this Amendment and Response to Restriction Requirement. However, if any additional fee is necessary, applicant hereby authorizes such fee to be charged to Deposit Account No. 50-2168.

Favorable action is respectfully requested.

Respectfully submitted,

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